REMARKS

Reconsideration is respectfully requested. Claims 1, 4, 9, 12, 15, 17, 18, 22-25 and 27-35 are pending. Claims 1, 9, 17, and 30-33 have been amended. Claims 2, 3, 5-8, 10, 11, 13, 14, 16, 19, 20, 21, and 26 have been canceled. Claims 18, 22-25 and 27-29 are withdrawn. New claims 34-36 have been added. No new matter has been added due to the amendments. Amendment to and cancellation of the claims does not affect inventorship.

Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim Amendments

Claims 1, 9, 17, and 30-33 have been amended. Support for the amendments to claims 1, 9, 32 and 33 can be found in the Specification at paragraphs [0089] and [0090]. Support for the amendments to claims 17, 30, 31 and new claims 34-36 can be found in Specification at paragraphs [00194] to [00196].

Objection to the Specification

The Examiner has objected to the Specification. Applicants respectfully traverse as follows:

The Examiner has objected to the Specification as being inconsistent as identifying the amino acid sequence of the atomic coordinate listing of FIG. 3 as SEQ ID NO:1. The Examiner states "[a]ccording to Figure 3, the first amino acid in the listing is Ala. However, the paper copy of the sequence listing identifies Met as the first amino acid of SEQ ID NO:1." Applicants traverse as follows:

FIG. 3 represents the structure coordinates of AIK as set forth in SEQ ID NO:1. As set forth in the legend, the amino acids of FIG. 3 are indicated by atom number (A) as well as amino acid number (E). Atom 1 in FIG. 3 (see column A) is derived from amino acid 126 (see column E), which is alanine (ALA). However, as set forth in the Specification at paragraph [00108] (as amended herein) and Table 7 of the Specification:

For some residues, the electron density obtained was insufficient to identify the side chain. As a result, the side chains of these residues were truncated such that a different amino acid is reported. Table 7 summarizes the differences between SEQ. ID No. 1 and the truncated residues appearing in Figure 3.

Table 7: Truncated Residues in The Structure Coordinates of Figure 3.

126R-126A	171K-170A	339K-339A
127Q-127A	175E-175A	375R-375A
170E-170A	183E-183A	

As is evident from SEQ ID NO:1, arginine (R) is the 126th amino acid residue of the AlK polypeptide. However, because of the insufficiency of the electron density obtained in the crystallography experiments, the reported data suggests that alanine is the 126th amino acid. However, this discrepancy has been explained by Applicants in the specification. Therefore, FIG. 3 accurately represents the atomic coordinate listing of the amino acid sequence set forth in SEQ ID NO: 1. Thus, the Examiner is respectfully requested to withdrawn the instant objection.

Claim Rejection - 35 U.S.C. § 112, First Paragraph

Claims 31-33 stand rejected under 35 U.S.C. § 112, first paragraph as containing new matter. Claims 1, 4, 9, 12, 15, 17 and 27-33 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description and enablement requirement. Applicants respectfully traverse as follows:

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575 (Fed.

Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375 (Fed. Cir. 1983)). **The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement.** *See* M.P.E.P. § 2163.02 (emphasis added).

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498,

I. New Matter

In raising the new matter rejection, the Examiner states:

> It is noted that there is no evidence in the record to support applicant's allegation that rTEV cleaves at a Gln-Gly junction. The arguments of counsel cannot take the place of evidence in the record....

Applicants respectfully traverse as follows:

It is important from the standpoint of avoiding the necessity for a patent specification to become a catalogue of existing technology. M.P.E.P. § 2182. A patent specification need not teach, and preferably omits, what is well known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986).

The properties of rTEV protease have been well known in the art since at least 1988. *See* attached article describing properties of rTEV protease. Therefore, after reviewing Applicants' disclosure (particularly the underlined portion in SEQ ID NO:3 set forth in FIG.1), one of ordinary skill in the art would readily conclude that cleavage of the polypeptide sequence of SEQ ID NO:3 with rTEV protease would release the first 23 residues of SEQ ID NO:3. Therefore, the limitation "residues 24-295 of SEQ ID NO:3" is not new matter.

II. Written Description and Enablement

Claims 1, 4, 9, 12, 15, 17 and 27-33 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description and enablement requirement.

Claims 27-29 are withdrawn thereby rendering the rejection moot with respect to these claims.

Without acquiescing to the propriety of the rejection, Applicants have amended claims 1 and 9 in order to clarify the scope of the claims. Therefore, Applicants request that the written description and enablement rejections with respect to claims 1, 4, 9, 12 and 15 be withdrawn.

Regarding claims 30 and 35, they are directed to a "non-crystalline" protein consisting of residues 125-391 of SEQ ID NO:1. As such, the claims do not encompass any crystalline forms of the protein. Support for claims 30 and 35 is in paragraphs [0070] and [00195] of the Specification, which specifically teaches the isolation and cloning of the portion of the gene encoding residues 125-391 of SEQ ID NO:1 into an expression vector.

Regarding claims 32 and 33, contrary to the Examiner's assertions, Applicants have not claimed any crystal containing residues 24-295 of SEQ ID NO:3, but rather have claimed crystals having specific space group and unit cell dimensions that are complexed with an inhibitor ligand. With respect to claim 32 and 33, SEQ ID NO:1 and SEQ ID NO:3 provide descriptions of protein sequences that comprise residues 24-295, while paragraphs [00197] to [00200] teach the methodology of crystallization of a protein.

Applicants have provided a working example for the crystallization of SEQ ID NO:3 which comprises residues 24-295 of SEQ ID NO:3. Based on the level of knowledge available at the time the application was filed in 2003 (see reference list below), coupled with Applicant's disclosure, a skilled artisan would be able to make the necessary adjustments to the experimental conditions to arrive at the appropriate crystallization conditions for a protein comprising residues 24-295 of SEQ ID NO:3.

A simple search on Google Scholar for references relating to protein crystallization methods yielded in excess of 30,000 hits most of which had a publication date prior to 2003. A sampling of the references is provided below. Therefore, it is quite clear that the level of skill in the art was high, with respect to crystallization methods, at the time the application was filed. Hence, a skilled artisan would have been more than capable of arriving at the conditions for crystallization of a protein comprising residues 24-295 of SEQ ID NO:3.

List of References

High-throughput protein crystallization - RC Stevens - Curr. Opin. Struct. Biol, **2000**

Overview of Protein Crystallization Methods- PC Weber - Methods in enzymology, **1997**

Comparative studies of protein crystallization by vapour-diffusion and microbatch techniques - NE Chayen - Acta Crystallogr D Biol Crystallogr, **1998**

An approach to rapid protein crystallization using nanodroplets - DC Uber, EW Cornell, RA Nordmeyer, WF Kolbe, J Jin - J Appl Crystallogr, **2002**

An automated system for micro-batch protein crystallization and screening - NE Chayen, PD Shaw Stewart, DL Maeder, DM Blow - Journal of Applied Crystallography, **1990**

Protein crystallization for genomics: towards high-throughput optimization techniques - NE Chayen, E Saridakis - Acta Crystallographica Section D Biological Crystallography, **2002**

Protein Crystallization - SD Durbin, G Feher - Annual Review of Physical Chemistry, **1996**

System for Evaluating Protein Crystallization Conditions by Microbatch and Vapor-Diffusion Methods - B Zheng, JD Tice, LS Roach, RF Ismagilov - Angewandte Chemie International Edition, 2004

Principles of Protein X-Ray Crystallography- J Drenth - **1999**

Screening of protein crystallization conditions on a microfluidic chip using nanoliter-size droplets - B Zheng, LS Roach, RF Ismagilov - J Am Chem Soc, **2003**

Protein interactions and crystallization- DF ROSENBAUM, CF ZUKOSKI - Journal of crystal growth, **1996**.

Protein Crystallization: Micro Techniques Involving Vapor Diffusion- DR Davies, DM Segal - Methods Enzymol, **1971**

Regarding claims 31 and 34, they are directed towards a "non-crystalline" protein consisting of residues 24-295 of SEQ ID NO:3. As such, the claims do not encompass any crystalline forms of the protein. Support for claims 31 and 34 is in paragraph [00196] of the Specification, which specifically teaches the cleavage of a fusion protein to generate a polypeptide consisting of residues 24-295 of SEQ ID NO:3 (see also discussion regarding new matter rejection above).

Regarding claims 17 and 36, they are directed towards a "non-crystalline" protein consisting of SEQ ID NO:3. Support for the claims can be found in paragraph [00196] of the Specification which teaches the expression of SEQ ID NO:3 as a fusion protein in an expression vector.

Therefore, the disclosure, taken in view of the level of skill in the art, fully describes the invention and enables a skilled artisan to practice the claimed invention without undue experimentation. As such, the rejections based on lacking of written description and enablement is improper and should be withdrawn.

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CONCLUSION

In view of the foregoing amendments and arguments, it is believed that all claims now pending in this application are in condition for allowance. Should the Examiner not agree, the Applicant respectfully asks the Examiner to contact the undersigned at the phone number below to discuss any remaining issues and accelerate the examination and allowance of this application. Authorization is granted to charge any outstanding fees due at this time for the continued prosecution of this matter to Morgan, Lewis & Bockius LLP Deposit Account No. 50-0310 (Client Matter No. 067450-5016US).

Respectfully submitted,
MORGAN, LEWIS & BOCKIUS LLP

Dated: 9/3/07

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